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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/524,399 | 02/11/2005 | Andreas Krause | TX/4-32608A | 6111 |

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CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

| EXAMINER | |
|---|---|
| DUNSTON, JENNIFER ANN | |
| ART UNIT | PAPER NUMBER |
| 1636 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/524,399 | KRAUSE ET AL. | |
| | Examiner | Art Unit | |
| | JENNIFER DUNSTON | 1636 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *26 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-3,8-11 and 15-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,8-11 and 15-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Appendix I*.

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/6/2009 has been entered.

Receipt is acknowledged of an amendment, filed 3/6/2009, in which claim 4 was canceled, claims 1, 3 and 8-11 were amended, and claims 15-18 were newly added. Claims 1-3, 8-11 and 15-18 are pending.

### *Election/Restrictions*

Applicant elected Group I without traverse in the reply filed 11/14/2008. Claims 1-3, 8-11 and 15-18 are under consideration.

### *Specification*

The disclosure is objected to because of the following informalities: at the paragraph bridging pages 10-11 of the specification, the sequence of the T7-polydT primer is referred to as "SEQ ID.: 1". Where the description or claims of a patent application discuss a sequence that is set forth in the Sequence Listing, reference must be made to the sequence by use of the sequence identifier, preceded by "**SEQ ID NO:**" in the text of the description or claims, even if the

sequence is also embedded in the text of the description or claims of the patent application. It would be remedial to replace the term "SEQ ID.: 1" with the term "SEQ ID NO: 1".

Appropriate correction is required.

The use of the trademarks GENBANK (paragraph bridging pages 1-2; page 2, 4th full paragraph; Tables 1, 2 and 4), GENECHIP (page 10, above the section titled "RNA amplification"; page 13 under the section titled "Washing Procedure"), RNEASY (page 10 under the section titled "RNA amplification"; page 12 above the section titled 'RNA fragmentation"), RIBOGREEN (page 10 under the section titled "RNA amplification"), SUPERSCRIPT (page 11), QIAQUICK (page 11) and TAQMAN (page 16) has been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17 and 18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection**.

New claims 17 and 18 were added in the amendment filed 3/6/2009. Claim 17 requires at least one renal allograft tissue biopsy sample to be obtained from the kidney transplanted subject in step b) of claim 3 "within 4 to 7 months after exposure to transplant therapy." Claim 18 requires at least one renal allograft tissue biopsy sample to be obtained from the kidney transplanted subject in step b) of claim 3 "at about 6 months after exposure to transplant therapy." Thus, the specification must provide literal or inherent support for obtaining a sample at 4 to 7 months or about 6 months relative to exposure to transplant therapy.

The response asserts that new claims 17 and 18 find support on page 4, "wherein the level of mRNA or protein encoded is preferably detected within 4 to 7 months post-transplantation, e.g., 6 months post-transplantation." With respect to the six month time point, the response asserts that support may be found in Tables 1-3, "which provide the genes differentially displayed in pre-chronic rejection ("CR") subjects versus control subjects at 6 months post transplant."

Page 4 of the specification refers to samples obtained 4 to 7 months or around 6 months relative to transplantation. The timing described in the specification is relative to the date of transplantation. Thus, the times are 4 to 7 months post-transplantation or about 6 months post transplantation.

The original specification, drawings and claims were thoroughly reviewed and no support could be found for the amendment of a range of time within which a sample is collected relative to exposure to transplant therapy. Accordingly, the amendment is a departure from the

specification and claims as originally filed, and the passages that Applicant has provided do not provide support.

Claims 1-3, 8-11 and 15-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. A rejection under 35 U.S.C. 112, first paragraph, was made in the prior action. The present rejection has been rewritten to address the amendments to the claims in the reply filed 3/6/2009.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

*Nature of the invention:* Claims 1, 2, 8-11, 15 and 16 are drawn to a method of early diagnosing chronic rejection (CR) in a kidney transplanted subject. Claim 1 sets forth the method steps of (a) assaying as a baseline value the levels of expression of the nucleic acid sequences set forth in SEQ ID NOs: 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38 (hereinafter referred to as SEQ ID NOs: 29-38), mRNA transcribed therefrom or protein encoded thereby in a renal allograft tissue biopsy obtained from a kidney transplanted control subject who is known not to develop CR; (b) assaying as a test value the "corresponding levels" of expression in a renal allograft tissue biopsy obtained from a kidney transplanted test subject within the first year post-

transplantation; and (c) comparing the baseline value of step (a) with the test value of step (b), wherein a baseline value lower than the test value, in the case of the levels of expression of the nucleic acid sequences set forth in SEQ ID NO: 29, 30, 31, 32, 33, 34, 35 or 36, mRNA transcribed therefrom or protein encoded thereby and higher than the test value, in the case of the levels of expression of the nucleic acid sequences set forth in SEQ ID NO: 37 or 38, mRNA transcribed therefrom or protein encoded thereby predicts that the kidney transplanted test subject has an increased risk of developing CR. Claim 2 limits the method to where the renal allograft tissue biopsy of the transplanted control subject is obtained from the control subject at the day of transplantation. Claims 8 and 9 limit the method to the detection of protein encoded by the nucleic acid sequences. Claims 10 and 11 limit the method to the detection of mRNA expression. Claim 15 limits the method to where the renal allograft tissue biopsy obtained from the kidney transplanted test subject in step (b) is obtained within 4-7 months post-transplantation. Claim 16 limits the method to where the renal allograft tissue biopsy obtained from the kidney transplanted test subject in step (b) is obtained around 6 months post-transplantation.

Claims 3, 17 and 18 are drawn to a method for monitoring in a kidney transplanted subject at risk of developing CR, comprising the steps of (a) assaying the levels of expression of the nucleic acid sequences set forth in SEQ ID NOs: 29-38, mRNA transcribed therefrom or protein encoded thereby in a renal allograft tissue biopsy sample obtained from a kidney transplanted subject prior to exposure to transplant therapy; (b) assaying the "corresponding" levels of expression in at least one renal allograft tissue biopsy sample obtained from the kidney transplanted subject after exposure to transplant therapy; and (c) comparing the levels of expression detected in step (a) and step (b), wherein an increase in the levels detected in step (b)

in comparison to the levels detected in step (a) in the case of the nucleic acid sequences set forth in SEQ ID N Os; 29, 30, 31, 32, 33, 34, 35 and 36, mRNA transcribed therefrom or protein encoded thereby and a decrease in the levels detected in step (b) in comparison to the levels detected in step (a) in the case of the levels of expression of the nucleic acid sequences set forth in SEQ ID NO: 37 and 38, mRNA transcribed therefrom or protein encoded thereby indicates an increased likelihood of developing CR.

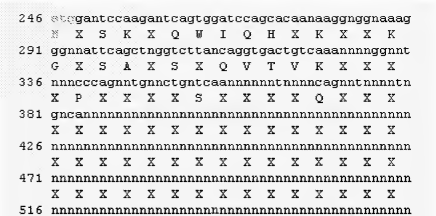
The nature of the invention is complex in that one must be capable of determining the level of mRNA transcribed from each of the recited sequences and the level of protein encoded by each of the recited sequences. Furthermore, one must be capable of determining level of mRNA transcribed from a sequence "corresponding" to each of the recited sequences and the level of protein encoded by a sequence "corresponding" to each of the recited sequences. The specification does not provide an explicit definition term "corresponding." Given the broadest reasonable interpretation of the term, the correspondence does not have to be direct (i.e., the sequences of SEQ ID NOs: 29-38). In other words, step (b) of the claims encompass measuring the expression levels of sequences of homologs or corresponding members of a gene family. Furthermore, the claims encompass the detection of SEQ ID NOs: 35 and 36 by reverse transcription PCR or quantitative PCR; however, the specification teaches that insufficient sequence data prevented the use of these methods W26469 (e.g., page 21). Moreover, the sequence of SEQ ID NO; 36 is mostly composed of undefined residues, which may be a, c, g or t. Thus, one would not know what protein is encoded by the sequence.

*Breadth of the claims:* The claims broadly encompass the measurement of the levels of expression from corresponding nucleic acid sequences.

*Guidance of the specification and existence of working examples:* The specification teaches the study of gene expression as part of a randomized, multicenter, double-blind, double-dummy, parallel group study in which serial renal protocol biopsies were taken at the time of transplantation (baseline), then 6 months and 12 months after transplantation (e.g., page 9, 1st full paragraph). The specification provides guidance with regard to the isolation of mRNA from the renal allograft tissue biopsies obtained from the kidney transplanted subjects and processing of the mRNA samples for hybridization to an Affymetrix oligonucleotide array (e.g., pages 9-14). To measure gene expression in the renal allograft tissue biopsies, processed aRNA was hybridized to an Affymetrix HG U95A v2 chip containing oligonucleotide probes for about 12,000 human genes (e.g., page 9, 2nd full paragraph). Statistical analysis was performed to determine the ability of the gene expression data to distinguish between the subjects who went on to develop CR and those that did not (e.g., pages 15-16). The specification teaches the use of the t and Wilcoxon statistics and the statistical measure described at page 15 to identify the genes that separate best the chronic rejection group from the control group (e.g., page 17, 1st paragraph). Applying the measures to each gene individually delivered a measure for the separation of the two groups, where the Q20/80 method identified 65 genes and the Q15/85 method identified 16 genes with complete separation of the (20%, 80%) and (15%, 85%) quantile ranges, respectively (e.g., page 17, 1st paragraph). Next, those genes were compared to the genes detected by the t- and Wilcoxon statistic, leading to the identification of 10 genes, which ranked among the 100 with most extreme t- and Wilcoxon statistic (e.g., page 17). Those gene identifiers and annotations are shown in Table 3. Using the Pearson Correlation, the set of 65 genes separates the two patient groups perfectly (e.g., page 18). When the set of 10 genes

was used, RNA expression profiles predicted the occurrence/non-occurrence of chronic rejection in 15 out of 17 patients (>88%) (e.g., page 18, last paragraph). Further, the set of 10 genes was also able to predict that a 12 month biopsy belonged to a patient that developed CR at month 18 (e.g., page 18, last paragraph). Accordingly, when the Affymetrix HG U95A v2 chip is uses to measure RNA expression for the 10 genes recited in Table 3, the method is predictive for chronic rejection. However, the claimed method requires measuring the expression level of mRNA transcribed from SEQ ID NO: 36 or protein encoded thereby. The specification teaches that there was insufficient sequence data to design TaqMan primers and probe for quantitative RT-PCR (e.g., Table 3).

*Predictability and state of the art:* It would be unpredictable to practice the claimed invention, because the specification and prior art do not teach one how to measure the mRNA transcribed from SEQ ID NO: 36 or protein encoded thereby. The specification describes the sequence of SEQ ID NO: 36 as GenBank Accession No. W26469, which is an uncharacterized expressed sequence tag (EST) designated 32f4 (e.g., Tables 3 and 6). If oligonucleotide probes were made from the sequence of SEQ ID NO: 36, those probes are likely to hybridize to different genes located on different human chromosomes (see the attached BLAST result in Appendix I). Furthermore, he longest "open reading frame" of the EST encodes a largely undefined protein, which is shown below.




Furthermore, the GenBank record for Accession No. W26469 indicates that the clone for the EST is not available. Thus, one would not be able to determine the expression levels by methods such as Northern blot analysis, reverse transcription PCR, real time quantitative PCR, or Western blot. Moreover, the probe sequences on the Affymetrix array that were capable of detecting differences in expression of the uncharacterized EST of SEQ ID NO: 36 are not taught by the specification.

*Amount of experimentation necessary:* Given the degenerate nature of the nucleotide sequence of SEQ ID NO: 36, it would require a large amount of experimentation to determine the identity of this sequence in a manner that would in some way enable the claimed invention. One embodiment of the method encompasses the use of an oligonucleotide array to detect the expression of SEQ ID NO: 36. However, the specification does not disclose the relationship

between the probe sequences on the Affymetrix Array used in the specification and the sequence of SEQ ID NO: 36. One would be required to test probes obtained from the sequence of SEQ ID NO: 36 for the ability to assay the expression of a gene, which is predictive for chronic rejection. Given that many different genes are likely to be detected by such probes, this is an unpredictable venture. Another embodiment of the method involves the use of quantitative PCR such as TaqMan. However, the specification teaches that TaqMan analysis was no performed due to the limited sequence information for W26469. Additional experimentation would be required to determine sufficient gene sequence to make and use primers and probes for quantitative detection of mRNA by RT-PCR. Identification of the gene from which the EST of W26469 is transcribed would also be required for any method based upon the analysis of protein encoded by the gene. The specification and prior art do not teach the protein sequence encoded by the gene from which EST ID 32f4 (W26469) is transcribed. Moreover, further experimentation would be assay genes that "correspond" to the nucleic acid sequences of SEQ ID NOs: 29-38 for the prediction of chronic rejection.

In view of the breadth of the claims and the lack of guidance provided by the specification as well as the unpredictability of the art, the skilled artisan would have required an undue amount of experimentation to make and/or use the claimed invention. Therefore, claims 1-3, 8-11 and 15-18 are not considered to be enabled by the instant specification.

Claims 1-3, 8-11 and 15-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. A rejection under 35 U.S.C. 112, first paragraph, was made in the prior action. The present rejection has been rewritten.

The claims encompass the provision of reagents to assay "corresponding levels of expression." The specification does not provide an explicit definition term "corresponding." Given the broadest reasonable interpretation of the term, the correspondence does not have to be direct (i.e., the sequences of SEQ ID NOs: 29-38). In other words, step (b) of the claims encompass measuring the expression levels of sequences of homologs or corresponding members of a gene family. Further, the claims require the provision of reagents to assay levels of expression of the nucleic acid sequence set forth in SEQ ID NO: 36, mRNA transcribed therefrom, or protein encoded thereby. The rejected claims thus require the description of sequences such that reagents can be designed to assay expression levels for the prediction of chronic rejection.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of a complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, and any combination thereof. The specification describes the sequence of SEQ ID NOs: 29-38. No description is provided of related homologs corresponding to these sequences, which are predictive for the occurrence or non-occurrence of chronic rejection in a kidney transplanted subject. Furthermore, the disclosure of the sequence of SEQ ID NO: 36 is not sufficient to allow one to envision the structure of those reagents that could be used to assay the levels of expression

of the gene, which is predictive for chronic allograft rejection. The specification describes the sequence of SEQ ID NO: 36 as GenBank Accession No. W26469, which is an uncharacterized expressed sequence tag (EST) designated 32f4 (e.g., Tables 3 and 6). If oligonucleotide probes were made from the sequence of SEQ ID NO: 36, those probes are likely to hybridize to different genes located on different human chromosomes (see the attached BLAST result in Appendix I). Furthermore, he longest "open reading frame" of the EST encodes a largely undefined protein, which is shown below.

```
246 xxggantccaagantcagtggatccagcacaanaaggnggnaaag
    X  X  S  K  X  Q  W  I  Q  H  X  K  X  X  K
291 ggnnattcagctnggtcttancaggtgactgtcaaannnnggnnt
    G  X  S  A  X  S  X  Q  V  T  V  K  X  X  X
336 nnncccagnntgnnctgntcaannnnnntnnnncagnntnnnntn
    X  P  X  X  X  X  S  X  X  X  X  Q  X  X  X
381 gncannnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnn
    X  X  X  X  X  X  X  X  X  X  X  X  X  X  X
426 nnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnn
    X  X  X  X  X  X  X  X  X  X  X  X  X  X  X
471 nnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnn
    X  X  X  X  X  X  X  X  X  X  X  X  X  X  X
516 nnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnn
    X  X  X  X  X  X  X  X  X  X  X  X  X  X  X
561 nnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnn
    X  X  X  X  X  X  X  X  X  X  X  X  X  X  X
606 nnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnn
    X  X  X  X  X  X  X  X  X  X  X  X  X  X  X
651 nnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnn
    X  X  X  X  X  X  X  X  X  X  X  X  X  X  X
696 nnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnnn
    X  X  X  X  X  X  X  X  X  X  X  X  X  X  X
741 nnnnnnnnnnngg 754
    X  X  X  X
```

Furthermore, the GenBank record for Accession No. W26469 indicates that the clone for the EST is not available. Thus, one would not be able to determine the expression levels by methods such as Northern blot analysis, reverse transcription PCR, real time quantitative PCR, or Western blot. Moreover, the probe sequences on the Affymetrix array that were capable of detecting

differences in expression of the uncharacterized EST of SEQ ID NO: 36 are not taught by the specification.

The prior art does not appear to offset the deficiencies of the instant specification in that it does not describe a set of corresponding sequences or the full sequence of EST ID 32f4.

*Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is now is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of sequences from which the reagents are designed, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation or identification. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18USPQ2d 1016.

Given the genus of corresponding sequences encompassed by the rejected claims, and given the limited description provided by the prior art and specification with regard to the sequences that are predictive for chronic allograft rejection, the skilled artisan would not have been able to envision a sufficient number of specific embodiments that meet the functional limitations of the claims to describe the genus of corresponding sequences. Furthermore, the

sequence of SEQ ID NO: 36 does not provide sufficient detail for one to envision the gene whose expression is predictive of chronic allograft rejection. Therefore, the skilled artisan would have reasonably concluded applicants were not in possession of the claimed invention for claims 1-3, 8-11 and 15-18.

***Response to Arguments - 35 USC § 112***

With respect to the rejection of claims 1-3, 8-11 and 15-18 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, Applicant's arguments filed 3/6/2009 have been fully considered but they are not persuasive.

The response notes that the amendments to the claims address a majority of the issues previously raised in the rejection under 35 U.S.C. 112, first paragraph. However, two issues remain: (i) use of the term "corresponding"; and (ii) one would not be able to assay the level of expression of the nucleic acid sequence set forth in SEQ ID NO: 36, mRNA transcribed therefrom or a protein encoded thereby.

With respect to the use of the term "corresponding," the response asserts that the claims have been amended to remove the phrase "corresponding to." This argument is not found persuasive. While the claims no longer recite "corresponding to," they do recite "corresponding levels of." To overcome this portion of the rejection, it would be remedial to explicitly refer to levels of expression of the nucleic acid sequences set forth in SEQ ID NOs: 29, 30, 31, 32, 33, 34, 35, 36, 37 and 38.

With respect to assaying the level of expression of the nucleic acid sequence set forth in SEQ ID NO: 36, mRNA transcribed therefrom or a protein encoded thereby, the response asserts

that one of ordinary skill in the art would certainly be able to do so without any undue experimentation. The response asserts that one could use the sequence of SEQ ID NO: 36 to design primers for Q-PCR, or could sequence the entirety of W26469, and use such sequence information for routine primer design.

These arguments are not found persuasive. The specification specifically teaches that there is insufficient sequence data for primer design for quantitative RT-PCR (e.g., Table 3 on page 21). The EST entry for W26469 indicates that a clone for this sequence is NOT available. Thus, one could not obtain a clone to determine the complete sequence and design reagents for the detection of mRNA or protein expression.

For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

With respect to the rejection of claims 1-3, 8-11 and 15-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, Applicant's arguments filed 3/6/2009 have been fully considered but they are not persuasive.

The response asserts that the claims have been amended to remove the phrase "corresponding to."

This argument is not found persuasive. While the claims no longer recite "corresponding to," they do recite "corresponding levels of." To overcome this portion of the rejection, it would be remedial to explicitly refer to levels of expression of the nucleic acid sequences set forth in SEQ ID NOs: 29, 30, 31, 32, 33, 34, 35, 36, 37 and 38.

The response asserts that there is no evidence on the record that sequences "corresponding to" SEQ ID NO: 36 were known in the art at the time the invention was made.

This argument is not found persuasive. Sequences from a number of different human chromosomes correspond to the sequence of SEQ ID NO: 36. See the attached BLAST results in Appendix I.

For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is 571-272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached at 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jennifer Dunston
Examiner
Art Unit 1636

/JD/

/ Christopher S. F. Low /
Supervisory Patent Examiner, Art Unit 1636